

[0208]

SEQUENCE LISTING

<110> Novartis AG, The Scripps Research Institute

<120> METHODS AND COMPOSITIONS ASSOCIATED WITH
NOCICEPTIVE PAIN

<130> 4-32851A/SCR

<150> US 06/434,540

<151> 2002-12-18

<160> 13

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<210> 1

<211> 320

<212> PRT

<213> Mus Musculus

<400> 1

Leu Asn Val Met Val Gln His Asn Arg Ile Glu Leu Leu Asn His Pro
 1 5 10 15
 Val Cys Arg Glu Tyr Leu Leu Met Lys Trp Cys Ala Tyr Gly Phe Arg
 20 25 30
 Ala His Met Met Asn Leu Gly Ser Tyr Cys Leu Gly Leu Ile Pro Met
 35 40 45
 Thr Leu Leu Val Val Lys Ile Gln Pro Gly Met Ala Phe Asn Ser Thr
 50 55 60
 Gly Ile Ile Asn Gly Thr Ser Ser Thr His Glu Glu Arg Ile Asp Thr
 65 70 75 80
 Leu Asn Ser Phe Pro Ile Lys Ile Cys Met Ile Leu Val Phe Leu Ser
 85 90 95
 Ser Ile Phe Gly Tyr Cys Lys Glu Val Ile Gln Ile Phe Gln Gln Lys
 100 105 110
 Arg Asn Tyr Phe Leu Asp Tyr Asn Asn Ala Leu Glu Trp Val Ile Tyr
 115 120 125
 Thr Thr Ser Ile Ile Phe Val Leu Pro Leu Phe Leu Asn Ile Pro Ala
 130 135 140
 Tyr Met Gln Trp Gln Cys Gly Ala Ile Ala Ile Phe Phe Tyr Trp Met

145 150 155 160
 Asn Phe Leu Leu Tyr Leu Gln Arg Phe Glu Asn Cys Gly Ile Phe Ile
 165 170 175
 Val Met Leu Glu Val Ile Phe Lys Thr Leu Leu Arg Ser Thr Gly Val
 180 185 190
 Phe Ile Phe Leu Leu Leu Ala Phe Gly Leu Ser Phe Tyr Val Leu Leu
 195 200 205
 Asn Phe Gln Asp Ala Phe Ser Thr Pro Leu Leu Ser Leu Ile Gln Thr
 210 215 220
 Phe Ser Met Met Leu Gly Asp Ile Asn Tyr Arg Asp Ala Phe Leu Glu
 225 230 235 240
 Pro Leu Phe Arg Asn Glu Leu Ala Tyr Pro Val Leu Thr Phe Gly Gln
 245 250 255
 Leu Ile Ala Phe Thr Met Phe Val Pro Ile Val Leu Met Asn Leu Leu
 260 265 270
 Ile Gly Leu Ala Val Gly Asp Ile Ala Glu Val Gln Lys His Ala Ser
 275 280 285
 Leu Lys Arg Ile Ala Met Gln Val Glu Leu His Thr Asn Leu Glu Lys
 290 295 300
 Lys Leu Pro Leu Trp Tyr Leu Arg Lys Val Asp Gln Arg Ser Thr Ile
 305 310 315 320

<210> 2

<211> 319

<212> PRT

<213> Homo sapiens

<400> 2

Leu Asn Ala Met Val Gln Asn Asn Arg Ile Glu Leu Leu Asn His Pro
 1 5 10 15
 Val Cys Lys Glu Tyr Leu Leu Met Lys Trp Leu Ala Tyr Gly Phe Arg
 20 25 30
 Ala His Met Met Asn Leu Gly Ser Tyr Cys Leu Gly Leu Ile Pro Met
 35 40 45
 Thr Ile Leu Val Val Asn Ile Lys Pro Gly Met Ala Phe Asn Ser Thr
 50 55 60
 Gly Ile Ile Asn Glu Thr Ser Asp His Ser Glu Ile Leu Asp Thr Thr
 65 70 75 80
 Asn Ser Tyr Leu Ile Lys Thr Cys Met Ile Leu Val Phe Leu Ser Ser
 85 90 95
 Ile Phe Gly Tyr Cys Lys Glu Ala Gly Gln Ile Phe Gln Gln Lys Arg
 100 105 110
 Asn Tyr Phe Met Asp Ile Ser Asn Val Leu Glu Trp Ile Ile Tyr Thr
 115 120 125

Thr Gly Ile Ile Phe Val Leu Pro Leu Phe Val Glu Ile Pro Ala His
 130 135 140
 Leu Gln Trp Gln Cys Gly Ala Ile Ala Val Tyr Phe Tyr Trp Met Asn
 145 150 155 160
 Phe Leu Leu Tyr Leu Gln Arg Phe Glu Asn Cys Gly Ile Phe Ile Val
 165 170 175
 Met Leu Glu Val Ile Leu Lys Thr Leu Leu Arg Ser Thr Val Val Phe
 180 185 190
 Ile Phe Leu Leu Leu Ala Phe Gly Leu Ser Phe Tyr Ile Leu Leu Asn
 195 200 205
 Leu Gln Asp Pro Phe Ser Ser Pro Leu Leu Ser Ile Ile Gln Thr Phe
 210 215 220
 Ser Met Met Leu Gly Asp Ile Asn Tyr Arg Glu Ser Phe Leu Glu Pro
 225 230 235 240
 Tyr Leu Arg Asn Glu Leu Ala His Pro Val Leu Ser Phe Ala Gln Leu
 245 250 255
 Val Ser Phe Thr Ile Phe Val Pro Ile Val Leu Met Asn Leu Leu Ile
 260 265 270
 Gly Leu Ala Val Gly Asp Ile Ala Glu Val Gln Lys His Ala Ser Leu
 275 280 285
 Lys Arg Ile Ala Met Gln Val Glu Leu His Thr Ser Leu Glu Lys Lys
 290 295 300
 Leu Pro Leu Trp Phe Leu Arg Lys Val Asp Gln Lys Ser Thr Ile
 305 310 315

<210> 3

<211> 352

<212> PRT

<213> *Drosophila melanogaster*

<400> 3

Leu Asn Thr Met Val Thr His Gly Arg Val Glu Leu Leu Ala His Pro
 1 5 10 15
 Leu Ser Gln Lys Tyr Leu Gln Met Lys Trp Asn Ser Tyr Gly Lys Tyr
 20 25 30
 Phe His Leu Ala Asn Leu Leu Ile Tyr Ser Ile Phe Leu Val Phe Val
 35 40 45
 Thr Ile Tyr Ser Ser Leu Met Met Asn Asn Ile Glu Leu Lys Ala Gly
 50 55 60
 Asp Asn Lys Thr Met Ser Gln Tyr Cys Asn Met Gly Trp Glu Gln Leu
 65 70 75 80
 Thr Met Asn Leu Ser Gln Asn Pro Ser Val Ala Ser Gln Ile Arg Leu
 85 90 95
 Asp Ser Cys Glu Glu Arg Ile Asn Arg Thr Thr Ala Ile Leu Phe Cys

100 105 110
 Ala Val Val Ile Val Val Tyr Ile Leu Leu Asn Ser Met Arg Glu Leu
 115 120 125
 Ile Gln Ile Tyr Gln Gln Lys Leu His Tyr Ile Leu Glu Thr Val Asn
 130 135 140
 Leu Ile Ser Trp Val Leu Tyr Ile Ser Ala Leu Val Met Val Thr Pro
 145 150 155 160
 Ala Phe Gln Pro Asp Gly Gly Ile Asn Thr Ile His Tyr Ser Ala Ala
 165 170 175
 Ser Ile Ala Val Phe Leu Ser Trp Phe Arg Leu Leu Leu Phe Leu Gln
 180 185 190
 Arg Phe Asp Gln Val Gly Ile Tyr Val Val Met Phe Leu Glu Ile Leu
 195 200 205
 Gln Thr Leu Ile Lys Val Leu Met Val Phe Ser Ile Leu Ile Ile Ala
 210 215 220
 Phe Gly Leu Ala Phe Tyr Ile Leu Leu Ser Lys Ile Ile Asp Pro Gln
 225 230 235 240
 Pro Asn His Leu Ser Phe Ser Asn Ile Pro Met Ser Leu Leu Arg Thr
 245 250 255
 Phe Ser Met Met Leu Gly Glu Leu Asp Phe Val Gly Thr Tyr Val Asn
 260 265 270
 Thr Tyr Tyr Arg Asp Gln Leu Lys Val Pro Met Thr Ser Phe Leu Ile
 275 280 285
 Leu Ser Val Phe Met Ile Leu Met Pro Ile Leu Leu Met Asn Leu Leu
 290 295 300
 Ile Gly Leu Ala Val Gly Asp Ile Glu Ser Val Arg Arg Asn Ala Gln
 305 310 315 320
 Leu Lys Arg Leu Ala Met Gln Val Val Leu His Thr Glu Leu Glu Arg
 325 330 335
 Lys Leu Pro His Val Trp Leu Gln Arg Val Asp Lys Met Glu Leu Ile
 340 345 350

<210> 4

<211> 368

<212> PRT

<213> *Drosophila melanogaster*

<400> 4

Leu Asp Val Leu Ile Glu Asn Glu Gln Lys Glu Val Ile Ala His Thr
 1 5 10 15
 Val Val Gln Arg Tyr Leu Gln Glu Leu Trp His Gly Ser Leu Thr Trp
 20 25 30
 Ala Ser Trp Lys Ile Leu Leu Leu Val Ala Phe Ile Val Cys Pro
 35 40 45

Pro Val Trp Ile Gly Phe Thr Phe Pro Met Gly His Lys Phe Asn Lys
 50 55 60
 Val Pro Ile Ile Lys Phe Met Ser Tyr Leu Thr Ser His Ile Tyr Leu
 65 70 75 80
 Met Ile His Leu Ser Ile Val Gly Ile Thr Pro Ile Tyr Pro Val Leu
 85 90 95
 Arg Leu Ser Leu Val Pro Tyr Trp Tyr Glu Val Gly Leu Leu Ile Trp
 100 105 110
 Leu Ser Gly Leu Leu Phe Glu Leu Thr Asn Pro Ser Asp Lys Ser
 115 120 125
 Gly Leu Gly Ser Ile Lys Val Leu Val Leu Leu Gly Met Ala Gly
 130 135 140
 Val Gly Val His Val Ser Ala Phe Leu Phe Val Ser Lys Glu Tyr Trp
 145 150 155 160
 Pro Thr Leu Val Tyr Cys Arg Asn Gln Cys Phe Ala Leu Ala Phe Leu
 165 170 175
 Leu Ala Cys Val Gln Ile Leu Asp Phe Leu Ser Phe His His Leu Phe
 180 185 190
 Gly Pro Trp Ala Ile Ile Ile Gly Asp Leu Leu Lys Asp Leu Ala Arg
 195 200 205
 Phe Leu Ala Val Leu Ala Ile Phe Val Phe Gly Phe Ser Met His Ile
 210 215 220
 Val Ala Leu Asn Gln Ser Phe Ala Asn Phe Ser Pro Glu Asp Leu Arg
 225 230 235 240
 Ser Phe Glu Lys Lys Asn Arg Asn Arg Gly Tyr Phe Ser Asp Val Arg
 245 250 255
 Met His Pro Ile Asn Ser Phe Glu Leu Leu Phe Phe Ala Val Phe Gly
 260 265 270
 Gln Thr Thr Thr Glu Gln Thr Gln Val Asp Lys Ile Lys Asn Val Ala
 275 280 285
 Thr Pro Thr Gln Pro Tyr Trp Val Glu Tyr Leu Phe Lys Ile Val Phe
 290 295 300
 Gly Ile Tyr Met Leu Val Ser Val Val Val Leu Ile Asn Leu Leu Ile
 305 310 315 320
 Ala Met Met Ser Asp Thr Tyr Gln Arg Ile Gln Val Val Leu Leu Asn
 325 330 335
 Ala Leu Leu Ser Asn Ser Thr Leu Phe Ile Asn Ser Tyr Phe Asn His
 340 345 350
 Lys Tyr Ile Asn Phe Ile Leu His Cys Val Leu Ile Ile Leu Tyr Phe
 355 360 365

<210> 5

<211> 365

<212> PRT

<213> *Caenorhabditis elegans*

<400> 5

Leu Asp Val Leu Ile Glu Asn Glu Gln Lys Glu Val Val Ser Tyr Ala
 1 5 10 15
 Ser Val Gln Arg Tyr Leu Thr Glu Val Trp Thr Ala Arg Val Asp Trp
 20 25 30
 Ser Phe Gly Lys Phe Val Ala Phe Ser Leu Phe Val Leu Ile Cys Pro
 35 40 45
 Pro Ala Trp Phe Tyr Phe Ser Leu Pro Leu Asp Ser Arg Ile Gly Arg
 50 55 60
 Ala Pro Ile Ile Lys Phe Val Cys His Ile Val Ser His Val Tyr Phe
 65 70 75 80
 Thr Ile Leu Leu Thr Ile Val Val Leu Asn Ile Thr His Lys Met Tyr
 85 90 95
 Glu Val Thr Ser Val Val Pro Asn Pro Val Glu Trp Leu Leu Leu Leu
 100 105 110
 Trp Leu Ser Gly Asn Leu Val Ser Glu Leu Ser Thr Val Gly Gly Gly
 115 120 125
 Ser Gly Leu Gly Ile Val Lys Val Leu Ile Leu Val Leu Ser Ala Met
 130 135 140
 Ala Ile Ala Val His Val Leu Ala Phe Leu Leu Pro Ala Val Phe Leu
 145 150 155 160
 Thr His Leu Asp Asn Asp Glu Lys Leu His Phe Ala Arg Thr Met Leu
 165 170 175
 Tyr Leu Lys Asn Gln Leu Phe Ala Phe Ala Leu Leu Phe Ala Phe Val
 180 185 190
 Glu Tyr Leu Asp Phe Leu Thr Val His His Leu Phe Gly Pro Trp Ala
 195 200 205
 Ile Ile Ile Arg Asp Leu Met Tyr Asp Leu Ala Arg Phe Leu Val Ile
 210 215 220
 Leu Met Leu Phe Val Ala Gly Phe Thr Leu His Val Thr Ser Ile Phe
 225 230 235 240
 Gln Pro Ala Tyr Gln Pro Val Asp Glu Asp Ser Ala Glu Leu Met Arg
 245 250 255
 Leu Ala Ser Pro Ser Gln Thr Leu Glu Met Leu Phe Phe Ser Leu Phe
 260 265 270
 Gly Leu Val Glu Pro Asp Ser Met Pro Pro Leu His Leu Val Pro Asp
 275 280 285
 Phe Ala Lys Ile Ile Leu Lys Leu Leu Phe Gly Ile Tyr Met Met Val
 290 295 300
 Thr Leu Ile Val Leu Ile Asn Leu Leu Ile Ala Met Met Ser Asp Thr
 305 310 315 320
 Tyr Gln Arg Ile Gln Ala Gln Ser Asp Lys Glu Trp Lys Phe Gly Arg
 325 330 335

Ala Ile Leu Ile Arg Gln Met Asn Lys Lys Ser Ala Thr Pro Ser Pro
 340 345 350
 Ile Asn Met Leu Thr Lys Leu Ile Ile Val Leu Arg Val
 355 360 365

<210> 6
 <211> 331
 <212> PRT
 <213> *Caenorhabditis elegans*

<400> 6
 Leu Lys Leu Met Ala Asp Ala Glu Lys Leu His Leu Leu Asn His Pro
 1 5 10 15
 Leu Ser Lys Ala Leu Leu Lys Tyr Lys Trp Asn Arg Leu Gly Arg Pro
 20 25 30
 Met Tyr Tyr Phe Ala Leu Phe Met Tyr Leu Val Phe Ile Val Ser Leu
 35 40 45
 Thr Gln Tyr Val Arg His Thr Lys Ala Pro Tyr Asn Val Trp Asn Glu
 50 55 60
 Glu Ser Tyr Tyr Asp Ser Glu Tyr Phe Asp Glu Asn Glu Thr Cys Pro
 65 70 75 80
 Gln Ile Asn Thr Thr Lys Pro Asp Val Val Trp Lys Ile Ile Ile Gln
 85 90 95
 Thr Leu Ala Val Cys Gln Ile Leu Val Glu Cys Phe Gln Leu Phe Gln
 100 105 110
 Arg Lys Phe Ala Tyr Leu Val Asn Trp Glu Asn Trp Ile Asp Cys Phe
 115 120 125
 Ile Tyr Ser Thr Ala Leu Ile Thr Val Tyr Asp Phe Ser Glu Cys Ser
 130 135 140
 Ala Thr Ser Gly Val Arg Gln Asn Trp Gln Trp Ile Leu Ala Ala Leu
 145 150 155 160
 Cys Ile Phe Phe Gly Trp Ile Asn Leu Leu Phe Met Ile Arg Lys Met
 165 170 175
 Pro Arg Phe Gly Ile Phe Val Val Met Phe Val Asp Ile Val Lys Thr
 180 185 190
 Phe Phe Arg Phe Phe Pro Val Phe Val Leu Phe Ile Ile Ala Phe Ser
 195 200 205
 Ser Ser Phe Tyr Val Ile Leu Gln Asn Arg Pro Glu Phe Ser Thr Ile
 210 215 220
 Phe Met Ser Pro Leu Lys Thr Thr Val Met Met Ile Gly Glu Phe Glu
 225 230 235 240
 Phe Thr Gly Ile Phe His Gly Asp Glu Thr Thr His Ala Glu Lys Met
 245 250 255
 Phe Gly Pro Ala His Thr Ala Val Ala Cys Ala Leu Phe Phe Phe Phe

260 265 270
 Cys Ile Ile Met Thr Ile Leu Leu Met Asn Leu Leu Val Gly Leu Ala
 275 280 285
 Val Asp Asp Ile Lys Gly Val Gln Glu Lys Ala Glu Leu Lys Arg Leu
 290 295 300
 Ala Met Gln Val Asp Leu Val Leu Gln Ile Glu Ala Ser Leu His Phe
 305 310 315 320
 Phe Ile Gln Arg Thr Lys Lys Tyr Ala Thr Cys
 325 330

<210> 7

<211> 333

<212> PRT

<213> *Drosophila melanogaster*

<400> 7

Leu Asn Thr Phe Val Asp Glu Gly Gln Lys Glu Ile Leu Glu His Pro
 1 5 10 15
 Leu Cys Ser Ser Phe Leu Tyr Ile Lys Trp Gly Lys Ile Arg Lys Tyr
 20 25 30
 Tyr Ile Gly Arg Leu Ile Phe Cys Phe Ser Phe Val Leu Phe Leu Thr
 35 40 45
 Leu Tyr Val Leu Thr Ala Leu Ala His Asn Cys Tyr Asn Gly Ser Lys
 50 55 60
 Asn Asp Asn Thr Thr Ile Pro Ala Gln Glu Leu Cys Gln Lys Gln Ser
 65 70 75 80
 Ile Leu Gly Asp Met Leu Arg Asn Asn Pro Phe Val Met Glu Met Gln
 85 90 95
 Trp Trp Val Leu Val Ala Ile Thr Ile Val Glu Ile Phe Arg Lys Leu
 100 105 110
 Tyr Gly Ile Thr Gly Tyr Ser Ser Phe Arg His Tyr Val Thr Gln Val
 115 120 125
 Glu Asn Ile Met Glu Trp Phe Val Ile Thr Ser Val Phe Val Ile Ser
 130 135 140
 Tyr Ile Tyr Thr Asn Lys Thr Tyr Thr Phe Gln Asn His Ile Gly Ala
 145 150 155 160
 Phe Ala Val Leu Leu Gly Trp Thr Asn Leu Met Leu Met Ile Gly Gln
 165 170 175
 Leu Pro Val Phe Asp Val Tyr Val Ala Met Tyr Thr Arg Val Gln Gly
 180 185 190
 Glu Phe Ala Lys Leu Phe Met Ala Tyr Ser Cys Met Leu Ile Gly Phe
 195 200 205
 Thr Ile Ser Phe Cys Val Ile Phe Pro Ser Ser Ser Ser Phe Ala Asn
 210 215 220

Pro Phe Met Gly Phe Ile Thr Val Leu Val Met Met Ile Gly Glu Gln
 225 230 235 240
 Asp Leu Ser Leu Leu Ile Asn Asp Pro Glu Gly Lys Asp Pro Pro Phe
 245 250 255
 Leu Leu Glu Val Ser Ala Gln Ile Thr Phe Val Leu Phe Leu Leu Phe
 260 265 270
 Val Thr Ile Ile Leu Met Asn Leu Leu Val Gly Ile Ala Val His Asp
 275 280 285
 Ile Gln Gly Leu Lys Lys Thr Ala Gly Leu Ser Lys Leu Val Arg Gln
 290 295 300
 Thr Lys Leu Ile Ser Tyr Ile Glu Ser Ala Leu Phe Asn Gly Tyr Leu
 305 310 315 320
 Pro Thr Trp Leu Arg Asn Leu Leu His Tyr Thr Ala Leu
 325 330

<210> 8

<211> 314

<212> PRT

<213> Drosophila melanogaster

<400> 8

Leu Leu Ser Leu Ile Glu Val Gly Gln Lys Arg Ile Leu Met His Pro
 1 5 10 15
 Leu Cys Glu Thr Phe Leu Phe Leu Lys Trp Arg Arg Ile Arg Lys Phe
 20 25 30
 Phe Leu Met Ser Leu Ala Tyr His Thr Leu Phe Val Ile Leu Phe Thr
 35 40 45
 Phe Tyr Val Ile Trp Val Tyr Val Arg Cys Cys Lys Lys Glu Glu Leu
 50 55 60
 Cys Val Ala Pro Gly Tyr Val Ser Thr Ile Gly Tyr Leu Val Ile Ile
 65 70 75 80
 Leu Asn Leu Ile Leu Leu Gly Lys Glu Val Phe Gln Met Ala His Gly
 85 90 95
 Leu Arg Gly Tyr Ala Lys Tyr Trp Glu Asn Trp Leu Gln Trp Thr Ile
 100 105 110
 Gly Thr Gly Val Leu Leu Cys Val Thr Pro Glu Thr Val Arg Thr Asp
 115 120 125
 Asp Leu Thr Ala Val Pro Val Trp Gln His His Val Ala Ala Ile Val
 130 135 140
 Ile Leu Leu Val Trp Leu Glu Leu Met Met Leu Val Gly Arg Phe Pro
 145 150 155 160
 Ile Phe Gly Val Tyr Val Gln Met Phe Thr Lys Val Ala Val Asn Phe
 165 170 175
 Ala Lys Phe Leu Leu Ala Tyr Ile Cys Leu Leu Val Ala Phe Gly Leu

180 185 190
 Ser Phe Ala Val Leu Phe Asn Asp Tyr Pro Ala Phe Glu Asn Ile Thr
 195 200 205
 Trp Ser Phe Leu Lys Ser Ile Thr Met Met Ser Gly Glu Leu Glu Phe
 210 215 220
 Glu Asp Ile Phe Tyr Gly Asp Tyr Ala Val Lys Phe Pro Val Thr Ala
 225 230 235 240
 His Ile Ile Phe Leu Ser Phe Val Leu Leu Val Thr Val Ile Leu Thr
 245 250 255
 Asn Leu Met Val Gly Leu Ala Val Ser Asp Ile Gln Gly Leu Gln Val
 260 265 270
 Ser Ala Thr Leu Asp Arg Leu Val Arg Gln Ala Glu Leu Val Ser Arg
 275 280 285
 Leu Glu Ser Leu Phe Phe Ser Arg Leu Leu Arg Ser Ala Pro Thr Asn
 290 295 300
 Leu Ile Gln Leu Cys Lys Arg Ser Ala Leu
 305 310

<210> 9

<211> 20

<212> DNA

<213> Mus Musculus

<400> 9

agtggggaga ctaccctgtg

20

<210> 10

<211> 21

<212> DNA

<213> Mus Musculus

<400> 10

tttatcatgc ccattcttg c

21

<210> 11

<211> 36

<212> DNA

<213> Mus Musculus

<400> 11

tttgatccg ccaccatgaa ggcgggcttg aggagg

36

<210> 12

<211> 37

<212> DNA

<213> Mus Musculus

<400> 12

tttgcggccg cctaaaagtc cgggtggcta atagaac

37

<210> 13

<211> 3378

<212> DNA

<213> Mus Musculus

<400> 13

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gaggatgaaa atctctgtcc tctgcatcac gcagcagcag aaggtaagt tgaactgatg 240
gaactgatca tcaatggttc ttcgttgtaa gtgctgaata taatggatgg ttatggaaat 300
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agccaccgg acttttag 3378